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EXAMINER	
KASSA, TIGABU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,604	HOLMES ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/16/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed December 16, 2008. **Claims 1-11 are currently pending. Claims 1-11 are under consideration in the instant office action.**

Withdrawn rejections:

Applicant's amendments and arguments filed on 12/16/08 are acknowledged and have been fully considered. The rejections applied under the second paragraph of 35 U.S.C. 112 in the previous office action are hereby withdrawn as a result of applicants claim amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention .

The rejection of claim 11 under 35 U.S.C. 112, first paragraph is maintained, because the specification, while being enabling for a method of treating infection of cattle with Cooperia or Ostertagia through the administration of the formulation, does not reasonably provide enablement for the prevention of infection of cattle with Cooperia or Ostertagia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope of breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack

thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1. *The breadth of the claim*: Claim 11 is drawn to a method of treating or preventing infection of cattle with Cooperia or Ostertagia using the anti-parasitic formulation. The scope of the claim is broad.
2. *Nature of the invention*: "Prevention" is interpreted in the absolute sense to mean no occurrence of parasitic infection. Claim 11 is drawn to a method of treating or preventing parasitic infection in animals by administering applicant's claimed formulation.
3. *The state of the prior art*: Method of treating parasitic infection in animals is well-known in the art using various formulations for example see Harvey (US Patent No. 6,165,987). However, the prior art is unequivocal with regards to prevention: "Despite substantial investment and research, the prevention of parasitic infections for example in humans is dependant of avoidance strategies since no vaccines are available" (www.merck.com/mmpe/print/sec14/ch181/ch181a.html). Additionally, the prior art teaches that compositions comprising anthelmintic agents can be used for treating parasitic infections in animals (for example see Harvey US Patent No. 6,165,987). Harvey is silent on prevention, which is interpreted as implying prevention is not in the purview of the prior art.

4. *Level of one of ordinary skill in the art*: One of ordinary skill in the art would include clinicians and scientists researching veterinary medicine (DVM).
5. *Level of predictability in the art*: There is relatively little unpredictability in the art with regards to treating versus preventing parasitic infection. Preventing parasitic infection using formulations is not currently possible.
6. *Amount of direction provided by the inventor*: Although, the instant specification discloses a method of treating parasitic infections in animals, applicants offer no guidance as to how to prevent parasitic infections using the claimed method.
7. *Existence of working examples*: The specification fails to provide scientific data and working embodiments with respect to prevention of parasitic infection.

Quantity or experimentation needed to make or use the invention based on the content of the disclosure: To use the invention as claimed, one of ordinary skill in the art would be required to conduct an undue amount of experimentation, to reasonably and accurately determine whether the composition and the corresponding method of the instant application does in fact prevent parasitic infection.

In conclusion, it is readily apparent from the aforementioned discussion, in conjunction with the lack of scientific data and working embodiments regarding the prevention of parasitic infection, that one of ordinary skill in the art would be required to conduct an undue amount of experimentation to determine how to prevent parasitic infection in cattle by administrating applicant's formulation.

Response to Arguments

Applicant's claim amendments and arguments filed 12/16/08 have been fully considered but they are not persuasive. Thus, the instant rejection is deemed to remain **proper and is maintained.**

Applicant has asserted that the instantly claimed invention is fully enabled for the prevention of infection of cattle with Cooperia or Ostertagia. Applicant's argument hinges first on the assertion that the specification does not have to contain any example with regard to the prevention of parasitic infections in cattle. Secondly, applicant's argument hinges on the assertion that based on the teachings of the specification one of the skilled artisan can extrapolate the dosage for treating infection of cattle to preventing infection. Finally, applicant argues that the examiner recited paragraphs from the Merck manual that relates to parasitic infections in humans not in cattle and also provided evidence for the prevention of parasitic infections in cattle from the Merck veterinary manual. The examiner fully considered all of the above arguments but found them to be not persuasive for the following reasons:

As applicants asserted the specification need not to contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA1970). However, applicants also should bear in mind that lack of a working example is a factor to be considered, especially in a case involving an unpredictable art such as the prevention of parasitic infections. The examiner argues that there is not enough evidence for the instantly claimed purpose namely "prevention of parasitic infections using the claimed formulations" in the prior art contrary to applicants assertion. Even the evidence provided by applicants from the

Merck Veterinary manual reiterate the examiner's findings reciting "strategic use of anthelmintics is designed **to reduce worm burdens** and thereby, the contamination of pastures". This recitation by the Merck veterinary manual clearly shows that the formulations are used for reducing damages by worm not completely thwarting (stopping) parasitic infections as what prevention literally means. A careful reading of the Merck Veterinary manual provided by applicant also recites "Effective worm control cannot always be achieved by drugs alone; however anthelmintics play an important role". This recitation is also an additional evidence for the formulations by themselves could not stop or prevent parasitic infections contrary to applicant assertions. With regard to the evidence provided by the examiner, the examiner reminds applicants that the evidence does not necessarily have to come from veterinary manual. The Merck manual recites "Despite substantial investment and research, the prevention of parasitic infections for example in humans is dependant of avoidance strategies since no vaccines are available". This recitation merely exemplifies humans, however, clearly does not necessarily exclude other animal species. Additionally, one of the skilled artisan can logically infer from the above recitation prevention of parasitic infection in cattle is also dependant of avoidance strategies. Therefore, due to lack of evidence in the prior art and also in the instant specification for the prevention of parasitic infections one of the skilled artisan has to perform an undue amount of experimentation contrary to applicants assertion.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 3-5, and 7-10 under 35 U.S.C. § 102(b) as being anticipated by Komer (US Patent No 5,773,422) is maintained.

Instant claim 1 recites a stable formulation for administration to animals including at least one anti-parasitic agent dissolved in a pyrrolidone solvent. In other embodiments, such as instant claim 3, the pyrrolidone solvent is 2-pyrrolidone or N-methyl pyrrolidone. Instant claim 4 recites that the avermectin or milbemycin is present in the range of between 0.01-5% w/v. In further limitations instant claim 5 recites in the formulation is selected from the list of abamectin, doramectin, eprinomectin, ivermectin, and moxidectin. Instant claim 7 recites the formulation additionally includes at least one medicament selected from the list recited in the instant claim. Instant claims 8-10 claim a formulation for administration to animals in a form for topical, parenteral, or oral administration.

Komer discloses novel formulations for the administration of an avermectin dissolved in N-methylpyrrolidone or 2-pyrrolidone or mixtures thereof (see Abstract and claim 1). This addresses the limitations recited in instant claims 1 and 3.

Komer discloses that the avermectin in the invented formulation is ivermectin, which is found in concentration of 1% (w/v) (column 3, lines 24-25 and claim 2). This addresses the limitations recited in instant claims 4 and 5.

Komer discloses the incorporation of other medicaments such as clorsulon, which is an additional active agent in the formulation in addition to ivermectin (column 4, lines 58-60). Furthermore, Komer also discloses the incorporation of methylparaben and propylparaben

(column 5, example 11), which are known preservatives that can be considered as other beneficial agents. This addresses the limitations recited in instant claim 7.

Komer discloses that the novel formulations are suitable for administration by intramuscular or subcutaneous injection, by topical application, stomach intubation, oral and drench administration (see Abstract). Furthermore, Komer discloses illustrative working examples for the different routes of administration, such as injectable, pour-on (topical) formulation, and oral formulations (see column 4, lines 30-67 and all column 5 and column 6, lines 1-31).

Response to Arguments

Applicant's claim amendments and arguments filed 11/17/08 have been fully considered but they are not persuasive. Thus, the instant rejection is deemed to remain **proper and is maintained.**

Applicant has asserted that Komer does not anticipate the invention of claims 1 and 3. Applicant's argument hinges on the interpretation of instant claim 1 as instantly written requires the formulation comprises levamisole and b at least one active selected from the group consisting of avermectins and milbemycins, wherein both of the said actives being dissolved in a pyrrolidone solvent. The examiner respectfully disagrees with applicants interpretation, **as written the claim can be interpreted as a stable formulation suitable for administration to animals comprising at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active is dissolved in a pyrrolidone solvent.** The examiner considered the list as a Markush group, therefore, a prior art disclosing a stable formulation comprising one of the disclosed anthelmintics anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

The rejection of claims 1 and 2 under 35 U.S.C. 103(a) as being unpatentable over Komer (US Patent No 5,773,422) in view of Huet et al. (US Patent No 6,426,333) and Harvey (US Patent No 6,165,987) is maintained.

Applicant Claims

Applicant claims a stable formulation as described above in the instant office action, wherein in some embodiments, such as in instant claim 2, the formulation further comprises an additional solvent selected from the glycol ethers.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Komer. Additionally, Komer teaches the formulation further comprises other cosolvents such as propylene glycol (column 3, lines 10-11)

Huet et al. disclose spot-on formulation for combating parasites comprising an effective amount of a 1-phenylpyrazole derivative; and/or, an effective amount of a macrocyclic lactone or antiparasitic agent; an acceptable liquid carrier vehicle; and optionally, a crystallization inhibitor (column 4, lines 39-67 and column 6, lines 1-30). Huet et al. disclose that "the liquid carrier vehicle comprises a solvent wherein the solvent is selected from the group consisting of, dipropylene glycol n-butyl ether, ethylene glycol monoethyl ether, ethylene glycol monomethyl ether, dipropylene glycol monomethyl ether, diethylene glycol monoethyl ether, which are glycol ethers (column 6, lines 5-20).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Komer lacks the teaching of formulations comprising glycol ethers as an additional solvent. This deficiency is cured by the teachings of Huet et al.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Komer by incorporating additional solvents like glycol ethers as taught by Huet et al., because Harvey discloses that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as glycol ethers to be bio-available; because the solid dosage forms are poorly absorbed by the animal (column 1, lines 22-25). The Harvey reference is used to demonstrate the general state of the art with regard to the use of solvents such as glycol ethers in anthelmintic formulations. Furthermore, the glycol ethers are commonly known solvents in the art for providing advantages of improved stability and extended shelf life to the formulations, when compared to solid dosage forms of said anthelmintics administered to animals. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Komer, Huet et al., and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections.

Response to Arguments

Applicant's claim amendments and arguments filed 12/16/09 have been fully considered but they are not persuasive. Thus, the instant rejection is deemed to remain **proper and is maintained.**

Applicant has asserted that the cited references do not teach or suggest the incorporation of levamisole. Applicant's argument hinges on the interpretation of instant claim 1 as instantly written requires the formulation comprises levamisole and b at least one active selected from the group consisting of avermictins and milbemycins, wherein both of the said actives being dissolved in a pyrrolidone solvent. The examiner respectfully disagrees with applicants

interpretation, **as written the claim can be interpreted as a stable formulation suitable for administration to animals comprising at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active is dissolved in a pyrrolidone solvent.** The examiner considered the list as a Markush group, therefore, a prior art disclosing a stable formulation comprising one of the disclosed anthelmintics anticipates the instant claims. Hence, the combinations of the teachings do not necessarily require the incorporation of levamisole. Therefore, as described above the combination of the teachings renders the instantly claimed invention obvious.

Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Komer (US Patent No 5,773,422) in view of Harvey (GB Patent Application No 2252730).

Applicant Claims

Applicant claims a stable formulation as described above wherein the composition comprises a levamisole that is present in the range of between 1-30% w/v.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Komer. Additionally, Komer teaches the incorporation of other medicaments, such as clorsulon, in the formulation in addition to ivermectin (column 4, lines 58-60).

Harvey (GB Patent Application No 2252730) teaches anthelmintic compositions containing praziquantel together with at least one other anthelmintic compound, for example levamisole (see abstract). Harvey (GB Patent Application No 2252730) also teaches a typical

formulation praziquantel from 0.5-15% w/v and levamisole 1-10% w/v (see page 3, general formulation) and gives an illustrative example (see page 4, example 1).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Komer lacks the teaching of formulations comprising levamisole in an amount of 1-30% w/v. This deficiency is cured by the teachings of Harvey (GB Patent Application No 2252730).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to ordinary skill in the art at the time of the instant invention to combine the teachings of Komer and Harvey, because Harvey discloses that formulations containing combinations of anthelmintic agents can be used to overcome drench resistance, which is caused by resistance to the effects of particular compounds (page 1, see background). For instance, Harvey discloses that ivermectin is active against parasitic roundworms but inactive against tapeworms (page 1, see background). A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because both Komer and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections.

Response to Arguments

Applicant's claim amendments and arguments filed 12/16/09 have been fully considered but they are not persuasive. Thus, the instant rejection is deemed to remain **proper and is maintained.**

Applicant has asserted that the cited references do not teach or suggest the incorporation of levamisole. Applicant's argument hinges on the interpretation of instant claim 1 as instantly written requires the formulation comprises levamisole and b at least one active selected from the group consisting of avermictins and milbemycins, wherein both of the said actives being dissolved in a pyrrolidone solvent. The examiner respectfully disagrees with applicants interpretation, **as written the claim can be interpreted as a stable formulation suitable for administration to animals comprising at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active is dissolved in a pyrrolidone solvent.** The examiner considered the list as a Markush group, therefore, a prior art disclosing a stable formulation comprising one of the disclosed anthelmintics anticipates the instant claims. Hence, the combinations of the teachings do not necessarily require the incorporation of levamisole, therefore, as described above the combination of the teachings renders the instantly claimed invention obvious.

Additionally, first applicants argue that Harvey relates to levamisole hydrochloride as a possible additional anthelmintic agent to be used in combination with praziquatel and not with avermictins and milbemycins. Secondly, applicants assert that Harvey teaches the levamisole in amounts of 1-10% w/v and do not teach or suggest the use of pyrrolidone solvent in the formulation, therefore, would not have rendered obvious claims 1 and 6. The examiner respectfully disagrees with applicants assertions, because the limitations for the incorporation of the pyrrolidone solvent and avermictin in the composition have been addressed by the teachings of Komer. Applicants are directed to the legal concept of *prima facie* obviousness to MPEP 2142. It is the combination of the teachings between the two references renders the instant claims

obvious as described above. Applicants should not attack only the teachings of one of the references, but should consider the teachings of both references in combination.

The rejection of claims 1 and 11 under 35 U.S.C. 103(a) as being unpatentable over Komer (US Patent No 5,773,422, Issued on June 30, 1998) in view of Harvey (US Patent No 6,165,987, IDS reference) is maintained.

Applicant Claims

Applicant claims a method of treating or preventing infection of cattle with Cooperia or Ostertagia by administering a formulation recited in claim 1, as described above in the instant office action.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Komer.

Harvey teaches "a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from the group comprising the avermectins and the milbemycins, and a suitable organic solvent selected from the group consisting of glycerol formal, ethyl lactate, benzyl alcohol and N-methyl-2-pyrrolidone and the like, wherein the composition is suitable for administration to warm-blooded non-human animals. The composition may be a solution or a paste and may be administered to the recipient animal by injection, drench or as an oral paste. A method of treating endo- and ectoparasites in non-human animals is also claimed" (see abstract and claim 13). Harvey (US Patent No 6,165,987) also discloses that "target parasite species were Haemonchus, Ostertagia,

Trichostrongulus, Cooperia, Nematodirus, Oesophagostomum, Chabertis and Monezia expansa" for treatment (column 10, lines 27-30). Ostertagia and Cooperia refer to two parasitic genera and that Harvey's method is suitable in the treatment of species of each genera. A species necessarily anticipates and obviates it corresponding genus.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Komer lacks the teaching of a method of treating or preventing infection of cattle with *Cooperia* or *Ostertagia* by administering a formulation recited in claim 1. This deficiency is cured by the teachings of Harvey.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time the instant invention was made to modify the method of Komer via treating parasitic infections caused by the species *Cooperia* or *Ostertagia* as taught by Harvey, because both *Cooperia* or *Ostertagia* are commonly known parasitic species that infect animals that are targeted for treatment by antiparasitic formulations as also demonstrated by Harvey. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because both Komer and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species like *Cooperia* or *Ostertagia*..

Response to Arguments

Applicant's claim amendments and arguments filed 11/17/08 have been fully considered but they are not persuasive. Thus, the instant rejection is deemed to remain **proper and is maintained.**

Applicants assert that one of skilled artisan would not have a reasonable expectation of success upon the combination of Komer and Harvey since the references do not address the difficulties of preparation of the claimed formulation and its stability in a non-aqueous solvent system. Additionally, applicants assert that the claimed combination of actives exhibited outstanding efficacy against all parasite species avoiding anthelminitic resistance. Finally, applicants also argue that the instant invention provides a stable formulation that can successfully treat the infections caused by all parasite species such as Cooperia, which is the key dose limiting parasite of the avermictin/milbemycin group, and Ostertagia, which is the key dose limiting parasite of the levamisole.

The examiner reminds applicants as written instant claim 1 can be interpreted as a stable formulation suitable for administration to animals comprising at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active is dissolved in a pyrrolidone solvent. The examiner considered the list as a Markush group, therefore, a prior art disclosing a stable formulation comprising one of the disclosed anthelmintics anticipates the instant claim. Bearing this point in mind, the examiner also reminds applicants instant claim 11 is a method of use not a method of making claim. The claim uses a comprising language that does not exclude the use of water in the composition. Additionally, absent surprising and unexpected results the stability of the formulations is within the purview of

the skilled artisan to be optimized. Finally, as described above instant claim 1 is anticipated by Komer and also Harvey clearly teaches a method of treating endo- and ectoparasites in non-human animals (see abstract and claim 13) such as *Cooperia* or *Ostertagia*. Therefore, one of the skilled artisan would have had a reasonable expectation of success upon the combination of Komer and Harvey within the same field of endeavor and address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species like *Cooperia* or *Ostertagia*.

New Rejections

Note: Based on applicants interpretation instant claim 1 recites **a stable formulation suitable for administration to animals comprising levamisole; and at least one active selected from the group consisting of avermectins, milbemycins, wherein the actives are dissolved in a pyrrolidone solvent. The examiner applied the following objections and new rejections based on this interpretation.**

Claim Objections

Claims 1-11 are objected due to the recitation of "A stable formulation suitable for administration to animals including at least one active selected from the group comprising avermectins and milbemycins and levamisole and both of said actives being dissolved in a pyrrolidone solvent." As written the claim did not follow proper idiomatic English and is also awkward. It would be remedial to applicants to correct the claim language with proper English. The examiner suggests that the claim may be rewritten as:

A stable formulation suitable for administration to animals comprising levamisole; and at least one active selected from the group consisting of avermectins and milbemycins, wherein the actives are dissolved in a pyrrolidone solvent.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As written instant claim 1 is vague and indefinite. It is not clear whether the claimed stable formulation comprises at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active agent is dissolved in pyrrolidone solvent or the claimed stable formulation comprises levamisole, and at least one active selected from the group

consisting of avermectins and milbemycins, wherein the active agents are dissolved in a pyrrolidone solvent.

The remaining claims 2-11 are rejected for depending on a rejected base claim (claim 1).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8, and 10 under 35 U.S.C. § 102(b) as being anticipated by Sorensen et al. (WO 01/05232).

Instant claim 1 recites a stable formulation suitable for administration to animals comprising levamisole; and at least one active selected from the group consisting of avermectins, milbemycins, wherein the actives are dissolved in a pyrrolidone solvent. In other embodiments, such as instant claim 3, the pyrrolidone solvent is 2-pyrrolidone or N-methyl pyrrolidone. Instant claim 4 recites that the avermectin or milbemycin is present in the range of between 0.01-5% w/v. In further limitations instant claim 5 recites in the formulation is selected from the list of abamectin, doramectin, eprinomectin, ivermectin, and moxidectin. Instant claim 6 recites a stable formulation as described in claim 1, wherein the composition comprises a levamisole that is present in the range of between 1-30% w/v. Instant claim 7 recites the formulation additionally includes at least one medicament selected from the list recited in the instant claim. Instant claims

8 and 10 claim a formulation for administration to animals in a form for topical or oral administration.

Sorensen et al. disclose a stable veterinary composition suitable for pour on or oral use as anthelmintic where a benzimidazole is carried in lactic acid, where preferably a co-solvent is present and that co-solvent is preferably N-methyl-2-pyrrolidone (page 3, lines 29). Sorensen et al. disclose an illustrative example of a composition comprising abamectin (0.10% w/v), levamisole HCl (3.75% w/v), triclabendazole (0.5% w/v) and other ingredients (page 7, lines 7-15). Sorensen et al. also disclose using the co-solvent such as N-methyl-2-pyrrolidone greatly increased the potential loading of the bezimidazole triclabendazole, which is anthelmentic agent (page 8, lines 5-7). These teachings clearly destroy the novelties of claims 1, 3-8, and 10.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10 above, and further in view of Huet et al. (US Patent No 6,426,333) and Harvey (US Patent No 6,165,987).

Applicant Claims

The claimed subject matters of instant claim 1 are set forth above. Instant claim 2 recites the formulation further comprises an additional co-solvent selected from the glycol ethers.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Sorensen et al.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Sorensen et al. lacks the teaching of formulations comprising glycol ethers as an additional solvent. This deficiency is cured by the teachings of Huet et al and Harvey.

Huet et al. disclose spot-on formulation for combating parasites comprising an effective amount of a 1-phenylpyrazole derivative; and/or, an effective amount of a macrocyclic lactone or antiparasitic agent; an acceptable liquid carrier vehicle; and optionally, a crystallization inhibitor (column 4, lines 39-67 and column 6, lines 1-30). Huet et al. disclose that "the liquid carrier vehicle comprises a solvent wherein the solvent is selected from the group consisting of, dipropylene glycol n-butyl ether, ethylene glycol monoethyl ether, ethylene glycol monomethyl ether, dipropylene glycol monomethyl ether, diethylene glycol monoethyl ether, which are glycol ethers (column 6, lines 5-20).

Harvey teaches that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as glycol ethers to be bio-available; because the solid dosage forms are poorly absorbed by the animal (column 1, lines 22-25).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. by incorporating additional solvents like glycol ethers as taught by Huet et al., because Harvey discloses that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as glycol ethers to be bio-available; because the solid dosage forms are poorly absorbed by the animal (column 1, lines 22-25). The Harvey reference is used to demonstrate the general state of the art with regard to the use of solvents such as glycol ethers in anthelmintic formulations. Furthermore, the glycol ethers are commonly known solvents in the art for providing advantages of improved stability and extended shelf life to the formulations, when compared to solid dosage

forms of said anthelmintics administered to animals. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al., Huet et al., and Harvey teach within the same field of endeavor and address the same problem, namely the treatment of parasitic infections.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10 above, and further in view of Komer (US Patent No 5,773,422).

Applicant Claims

The claimed subject matters of instant claim 1 are set forth above. Instant claim 9 recites the formulation of claim 1 being suitable for parenteral administration.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Sorensen et al.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Sorensen et al. does not explicitly teach the composition being used for parenteral administration. This deficiency is cured by the teachings of Komer.

Komer discloses that the avermectin in the invented formulation is ivermectin, which is found in concentration of 1% (w/v) (column 3, lines 24-25 and claim 2). This addresses the limitations recited in instant claims 4 and 5.

Komer discloses that the novel formulations are suitable for administration by intramuscular or subcutaneous injection, by topical application, stomach intubation, oral and drench administration (see Abstract). Furthermore, Komer discloses illustrative working examples for the different routes of administration, such as injectable, pour-on (topical) formulation, and oral formulations (see column 4, lines 30-67 and all column 5 and column 6, lines 1-31).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. by preparing it for parenteral administration, because Komer teaches formulations containing anthelmintic agents for parenteral administration. One of ordinary skilled artisan would be motivated to have such a composition for parenteral administration, because it is a conventionally known administration system. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because Sorensen et al. and Komer teach similar compositions for similar purposes namely control of parasitic infections.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10 above, and further in view of Harvey (US Patent No 6,165,987, IDS reference).

Applicant Claims

Applicant claims a method of treating or preventing infection of cattle with Cooperia or Ostertagia by administering a formulation recited in claim 1.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

As discussed above the required limitations of instant claim 1 are addressed by the teachings of Sorensen et al.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Although Sorensen et al. teach a method of treating a ruminant mammal for nematodes, trematodes and/or cestodes comprising orally administering the formulation taught above, Sorensen et al. lack the teaching of a method of treating or preventing infection of cattle with *Cooperia* or *Ostertagia* by administering a formulation recited in claim 1. This deficiency is cured by the teachings of Harvey.

Harvey teaches "a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from the group comprising the avermectins and the milbemycins, and a suitable organic solvent selected from the group consisting of glycerol formal, ethyl lactate, benzyl alcohol and N-methyl-2-pyrrolidone and the like, wherein the composition is suitable for administration to warm-blooded non-human animals. The composition may be a solution or a paste and may be administered to the recipient animal by injection, drench or as an oral paste. A method of treating endo- and ectoparasites in

non-human animals is also claimed" (see abstract and claim 13). Harvey (US Patent No 6,165,987) also discloses that "target parasite species were Haemonchus, Ostertagia, Trichostrongulus, Cooperia, Nematodirus, Oesophagostomum, Chabertis and Monezia expansa" for treatment (column 10, lines 27-30). Ostertagia and Cooperia refer to two parasitic genera and that Harvey's method is suitable in the treatment of species of each genera. A species necessarily anticipates and obviates it corresponding genus.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art at the time the instant invention was made to modify the method of Sorensen et al. via treating parasitic infections caused by the species *Cooperia* or *Ostertagia* as taught by Harvey, because both *Cooperia* or *Ostertagia* are commonly known parasitic species that infect animals that are targeted for treatment by antiparasitic formulations as also demonstrated by Harvey. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings because both Sorensen et al. and Harvey address the same problem, namely the treatment of parasitic infections, which are caused by the parasitic species.

Conclusion

Claims 1-11 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 3/25/09

/Mina Haghighatian/
Primary Examiner, Art Unit 1616